## (19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 6 October 2005 (06.10.2005)

**PCT** 

## (10) International Publication Number WO 2005/092835 A1

(51) International Patent Classification<sup>7</sup>: C07C 217/20, C07D 295/12, C07C 323/25, 55/10, 53/18, A61K 31/13, 31/40, A61P 25/00

(21) International Application Number:

PCT/US2005/005226

(22) International Filing Date: 18 February 2005 (18.02.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(**30**) **Priority Data:** 60/550,259

5 March 2004 (05.03.2004) US

(71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, Indiana 46285 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BOULET, Serge, Louis [US/US]; 10813 Windemere Boulevard, Fishers,

Indiana 46038 (US). **JOHANSSON**, **Anette**, **Margareta** [SE/US]; 6350 Brokenhurst Road, Indianapolis, Indiana 46220 (US). **SMITH**, **Sarah**, **Marie** [US/US]; 50 North Sadlier Drive, Indianapolis, Indiana 46219 (US).

(74) Agents: GAYLO, Paul, J. et al.; ELI LILLY AND COM-PANY, P. O. Box 6288, Indianapolis, Indiana 46206-6288 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

[Continued on next page]

(54) Title: PHARMACEUTICAL COMPOUNDS

$$X$$
 $A$ 
 $Y$ 
 $NR_1R_2$ 

$$R_3$$
  $R_4$   $R_5$   $R_5$   $R_6$   $R_6$   $R_7$   $R_8$   $R_7$   $R_8$   $R_8$   $R_7$   $R_8$   $R_8$   $R_7$   $R_8$   $R_8$   $R_8$   $R_7$   $R_8$   $R_8$   $R_8$   $R_7$   $R_8$   $R_8$   $R_9$   $R_9$ 

(57) **Abstract:** The present invention relates to inhibitors of serotonin and/or norepinephrine reuptake and specifically provides compounds of formula (I): wherein A is selected from -O- and -S-; X is selected from C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>2</sub>-C<sub>8</sub> alkenyl, and C<sub>4</sub>-C<sub>8</sub> cycloalkylalkyl, each of which may be optionally substituted with up to 3 substituents each independently selected from phenyl, pyrrolidinyl, piperidinyl, morpholinyl, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl-S(O)<sub>n</sub>- where n is 0, 1 or 2, -CF<sub>3</sub>, -CN and -CONH<sub>2</sub>; Y is selected from (a), (b), (c), (d), (e), (f) where R<sub>3</sub>, R<sub>4</sub>and R<sub>5</sub> are independently selected from hydrogen, halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkyl-S(O)<sub>n</sub>- where n is 0, 1 or 2, nitro, acetyl, -CF<sub>3</sub>, -SCF<sub>3</sub> and cyano; R<sub>6</sub> and R<sub>7</sub> are independently selected from halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkyl-S(O)<sub>n</sub>- where n is 0, 1 or 2, nitro, acetyl, -CF<sub>3</sub>, -SCF<sub>3</sub> and cyano; R<sub>8</sub> is selected from chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkyl-S(O)<sub>n</sub>- where n is 0, 1 or 2, nitro, acetyl, -CF<sub>3</sub>, -SCF<sub>3</sub> and cyano; R<sub>1</sub> and R<sub>2</sub> are each independently hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; or pharmaceutically acceptable salts thereof; or compositions thereof and methods of using the same.





European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## **Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,

EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

## **Published:**

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.